

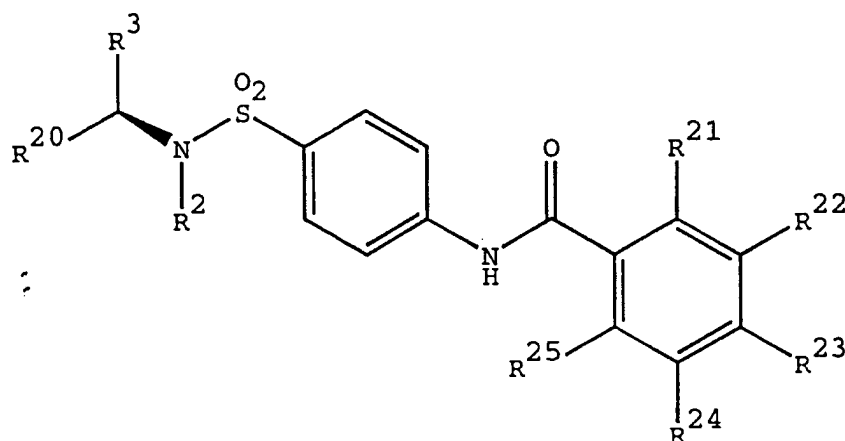
WO 01/05389

PCT/US00/16323

CLAIMS

What is claimed is:

1. A matrix metalloproteinase inhibiting compound  
5 having the structure:



10 or a salt, an enantiomer, a diastereomer, a  
racemate, or a tautomer thereof, wherein:

R<sup>2</sup> is selected from the group consisting of H,  
alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl,  
alkylaryl, arylalkyl, alkoxyalkyl, hydroxyalkyl,  
15 aminoalkyl, alkylaminoalkyl, heterocycloalkyl,  
and heterocycloalkylalkyl;

R<sup>3</sup> is selected from the group consisting of H,  
alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl,  
alkylaryl, arylalkyl, alkoxy, alkoxyalkyl,  
hydroxyalkyl, aminoalkyl, alkylaminoalkyl,  
20 haloalkoxy, haloalkylthio, and heterocycloalkyl;

R<sup>20</sup> is selected from the group consisting of  
-C(O)OH, -C(O)NHOH, -SH, and -C(O)SH; and

R<sup>21</sup>, R<sup>22</sup>, R<sup>23</sup>, R<sup>24</sup>, and R<sup>25</sup> are independently  
selected from the group consisting of H, C<sub>1</sub> to  
25 about C<sub>20</sub> alkyl, C<sub>1</sub> to about C<sub>20</sub> alkenyl, C<sub>1</sub> to  
about C<sub>20</sub> alkynyl, cycloalkyl, haloalkyl,  
alkoxyalkyl, hydroxyalkyl, aminoalkyl,

WO 01/05389

PCT/US00/16323

alkylaminoalkyl, nitroalkyl, heterocycloalkyl,  
alkoxy, cycloalkoxy, alkoxycarbonyl,  
alkoxyalkyl, haloalkoxy, haloalkylthio,  
alkylamino, and carboxyalkyl.

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2. The matrix metalloproteinase inhibiting compound  
of claim 1 wherein  $R^{20}$  is selected from the group  
consisting of  $-C(O)OH$  and  $-C(O)NHOH$ .

10

3. The matrix metalloproteinase inhibiting compound  
of claim 2 wherein  $R^{21}$  and  $R^{25}$  are H.

4. The matrix metalloproteinase inhibiting compound  
of claim 3 wherein  $R^{22}$  and  $R^{24}$  are H.

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5. The matrix metalloproteinase inhibiting compound  
of claim 4 wherein  $R^{23}$  is  $C_1$  to about  $C_{20}$  alkyl.

20

6. The matrix metalloproteinase inhibiting compound  
of claim 5 wherein  $R^{23}$  is  $C_1$  to about  $C_{20}$  linear  
alkyl.

25

7. The matrix metalloproteinase inhibiting compound  
of claim 2 wherein  $R^{20}$  is  $-C(O)OH$ .

30

8. The matrix metalloproteinase inhibiting compound  
of claim 7 wherein  $R^3$  is selected from the group  
consisting of alkyl, alkenyl, alkynyl,  
haloalkoxy, haloalkylthio, and heterocycloalkyl.

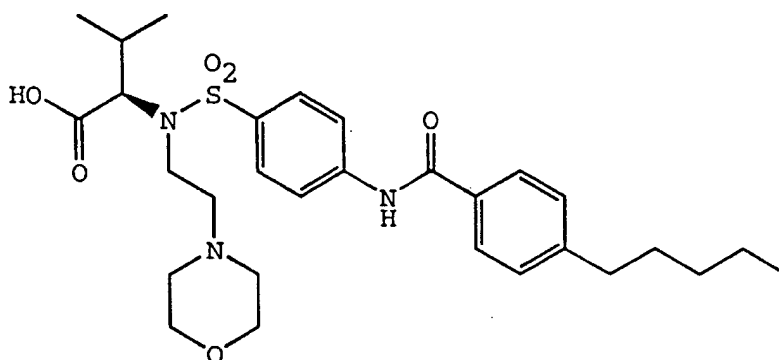
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9. The matrix metalloproteinase inhibiting compound  
of claim 8 wherein  $R^3$  is heterocycloalkyl.
10. The matrix metalloproteinase inhibiting compound  
of claim 9 wherein  $R^3$  is 2-(N-morpholino)ethyl.

WO 01/05389

PCT/US00/16323

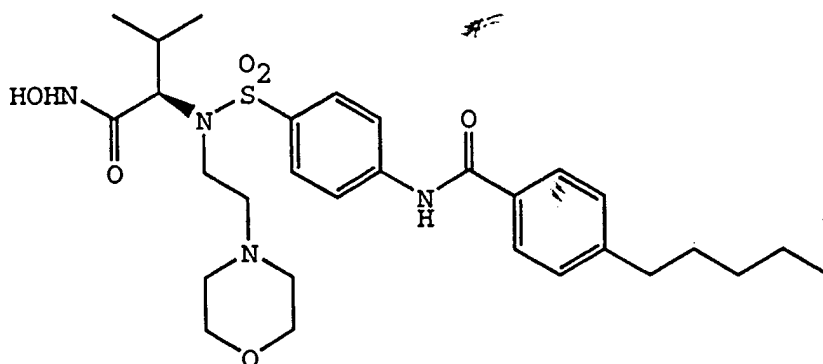
11. The matrix metalloproteinase inhibiting compound of claim 2 wherein  $R^{20}$  is  $-C(O)NHOH$ .
12. The matrix metalloproteinase inhibiting compound of claim 11 wherein  $R^3$  is selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkoxy, haloalkylthio, and heterocycloalkyl.
13. The matrix metalloproteinase inhibiting compound of claim 12 wherein  $R^3$  is heterocycloalkyl.
14. The matrix metalloproteinase inhibiting compound of claim 13 wherein  $R^3$  is 2-(N-morpholino)ethyl.
15. The matrix metalloproteinase inhibiting compound of claim 14 having the structure



- or a salt, an enantiomer, a racemate, or a tautomer thereof.
16. The matrix metalloproteinase inhibiting compound of claim 14 having the structure

WO 01/05389

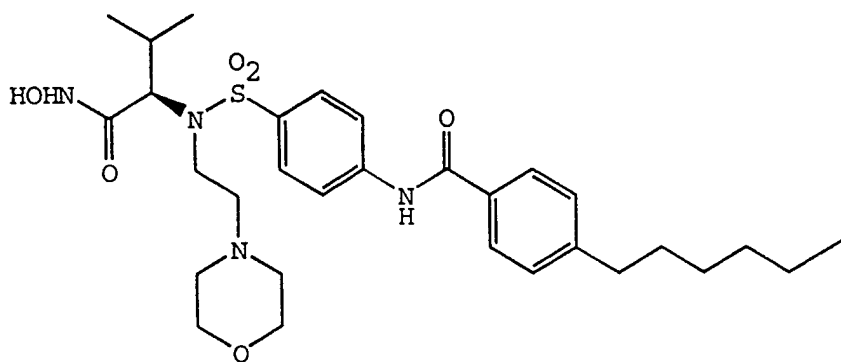
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or a salt, an enantiomer, a racemate, or a tautomer thereof.

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17. The matrix metalloproteinase inhibiting compound of claim 14 having the structure



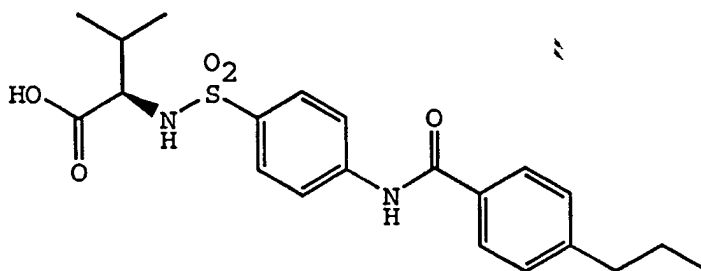
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or a salt, an enantiomer, a racemate, or a tautomer thereof.

WO 01/05389

PCT/US00/16323

18. The matrix metalloproteinase-inhibiting compound of claim 14 having the structure

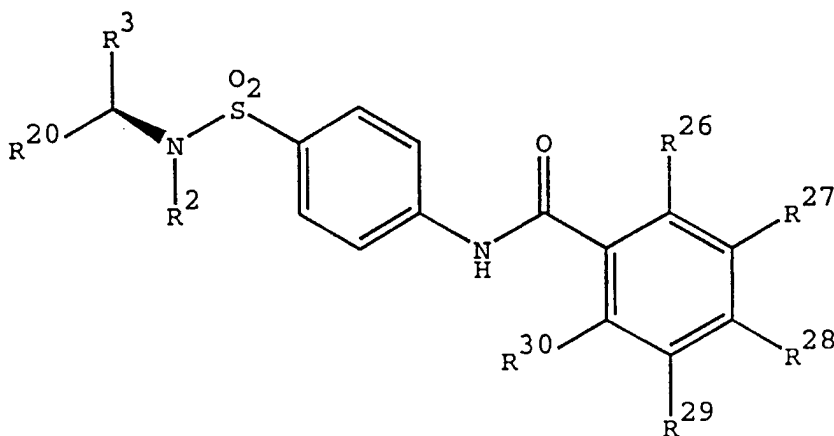


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or a salt, an enantiomer, a racemate, or a tautomer thereof.

19. A method of changing the conformation of a matrix metalloproteinase wherein the method comprises contacting the matrix metalloproteinase with a compound having the formula:

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or a salt, an enantiomer, a diastereomer, a racemate, or a tautomer thereof, thereby changing the conformation of the matrix metalloproteinase, wherein:

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$R^2$  is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl,

WO 01/05389

PCT/US00/16323

alkylaryl, arylalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, heterocycloalkyl, and heterocycloalkylalkyl;

5  $R^3$  is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, haloalkoxy, haloalkylthio, and heterocycloalkyl;

10  $R^{20}$  is selected from the group consisting of -C(O)OH, -C(O)NHOH, -SH, and -C(O)SH; and

$R^{26}$ ,  $R^{27}$ ,  $R^{28}$ ,  $R^{29}$ , and  $R^{30}$  are independently selected from the group consisting of about  $C_3$  to about  $C_{20}$  alkyl, about  $C_3$  to about  $C_{20}$  alkenyl, about  $C_3$  to about  $C_{20}$  alkynyl, cycloalkyl, 15 haloalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, nitroalkyl, heterocycloalkyl, alkoxy, cycloalkoxy, alkoxycarbonyl, alkoxyalkyl, haloalkoxy, haloalkylthio, alkylamino, and carboxyalkyl.

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20. The method of claim 19 wherein  $R^{20}$  is selected from the group consisting of -C(O)OH and -C(O)NHOH.

25 21. The method of claim 19 wherein  $R^3$  is selected from the group consisting of H, alkyl, alkenyl, alkynyl, haloalkoxy, haloalkylthio, and heterocycloalkyl

30 22. The method of claim 21 wherein  $R^3$  is a  $C_1$  to about  $C_{12}$  alkyl.

23. The method of claim 22 wherein  $R^3$  is a  $C_1$  to about  $C_4$  alkyl.

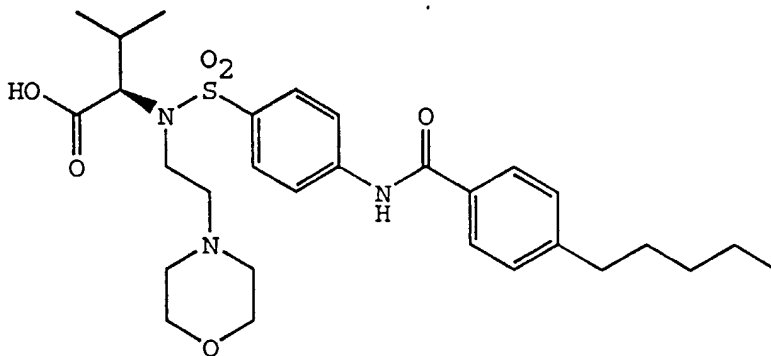
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24. The method of claim 23 wherein  $R^3$  is isopropyl.

WO 01/05389

PCT/US00/16323

25. The method of claim 19 wherein  $R^2$  is heterocycloalkylalkyl.
- 5 26. The method of claim 25 wherein  $R^3$  is 2-(N-morpholino)ethyl.
27. The method of claim 19 wherein  $R^{26}$  and  $R^{30}$  are H.
- 10 28. The method of claim 27 wherein  $R^{27}$  and  $R^{29}$  are H.
29. The method of claim 28 wherein  $R^{28}$  is about  $C_3$  to about  $C_{20}$  alkyl.
- 15 30. The method of claim 29 wherein  $R^{28}$  is about  $C_3$  to about  $C_{20}$  linear alkyl.
31. The method of claim 30 wherein  $R^{28}$  is selected from the group consisting of n-propyl, n-butyl, 20 n-pentyl and n-hexyl.
32. The method of claim 31 wherein the compound has the structure:

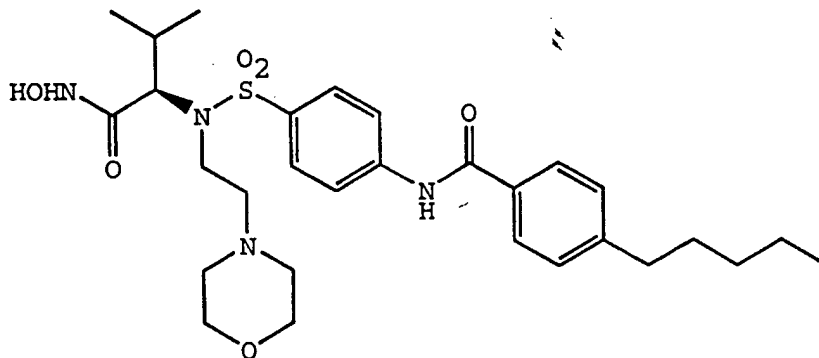


or a salt, an enantiomer, a racemate, or a tautomer thereof.

WO 01/05389

PCT/US00/16323

33. The method of claim 31 wherein the compound has the structure:

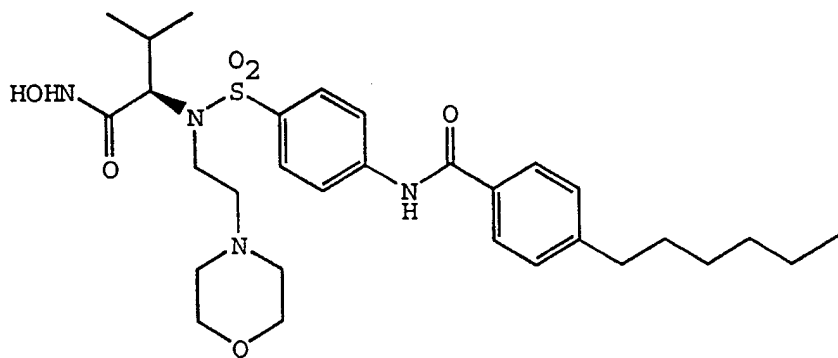


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or a salt, an enantiomer, a racemate, or a tautomer thereof.

34. The method of claim 31 wherein the compound has the structure:

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or a salt, an enantiomer, a racemate, or a tautomer thereof.

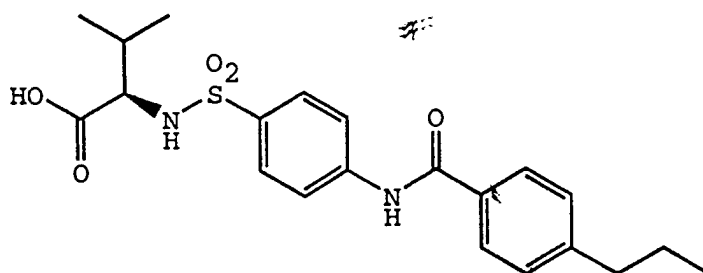
35. The method of claim 31 wherein the compound has the structure:

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WO 01/05389

PCT/US00/16323



or a salt, an enantiomer, a racemate, or a tautomer thereof.

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36. The method of claim 19 wherein the matrix metalloproteinase is selected from the group consisting of MMP-8 and MMP-13.

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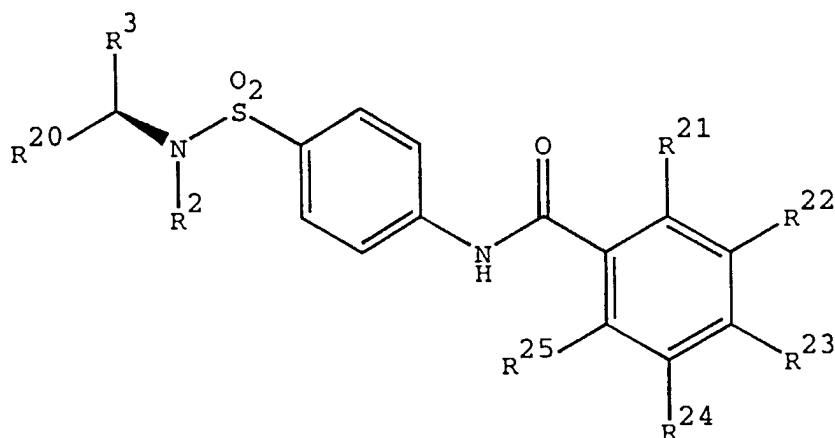
37. The method of claim 36 wherein the matrix metalloproteinase is MMP-8.

38. The method of claim 36 wherein the matrix metalloproteinase is MMP-13.

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39. A method of inhibiting a matrix metalloproteinase wherein the method comprises contacting the matrix metalloproteinase with a compound having the formula:

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WO 01/05389

PCT/US00/16323

or a salt, an enantiomer, a diastereomer, a  
racemate, or a tautomer thereof, thereby  
inhibiting the matrix metalloproteinase,  
5 wherein:

$R^2$  is selected from the group consisting of H,  
alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl,  
alkylaryl, arylalkyl, alkoxyalkyl, hydroxyalkyl,  
aminoalkyl, alkylaminoalkyl, heterocycloalkyl,  
10 and heterocycloalkylalkyl;

$R^3$  is selected from the group consisting of H,  
alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl,  
alkylaryl, arylalkyl, alkoxy, alkoxyalkyl,  
hydroxyalkyl, aminoalkyl, alkylaminoalkyl,  
15 haloalkoxy, haloalkylthio, and heterocycloalkyl;

$R^{20}$  is selected from the group consisting of  
-C(O)OH, -C(O)NHOH, -SH, and -C(O)SH; and

$R^{21}$ ,  $R^{22}$ ,  $R^{23}$ ,  $R^{24}$ , and  $R^{25}$  are independently  
selected from the group consisting of H,  $C_1$  to  
20 about  $C_{20}$  alkyl,  $C_1$  to about  $C_{20}$  alkenyl,  $C_1$  to  
about  $C_{20}$  alkynyl, cycloalkyl, haloalkyl,  
alkoxyalkyl, hydroxyalkyl, aminoalkyl,  
alkylaminoalkyl, nitroalkyl, heterocycloalkyl,  
alkoxy, cycloalkoxy, alkoxycarbonyl,  
25 alkoxyalkyl, haloalkoxy, haloalkylthio,  
alkylamino, and carboxyalkyl.

40. The method of claim 39 wherein  $R^{20}$  is selected  
from the group consisting of -C(O)OH and  
30 -C(O)NHOH.

41. The method of claim 39 wherein  $R^3$  is selected  
from the group consisting of H, alkyl, alkenyl,  
alkynyl, haloalkoxy, haloalkylthio, and  
35 heterocycloalkyl.

WO 01/05389

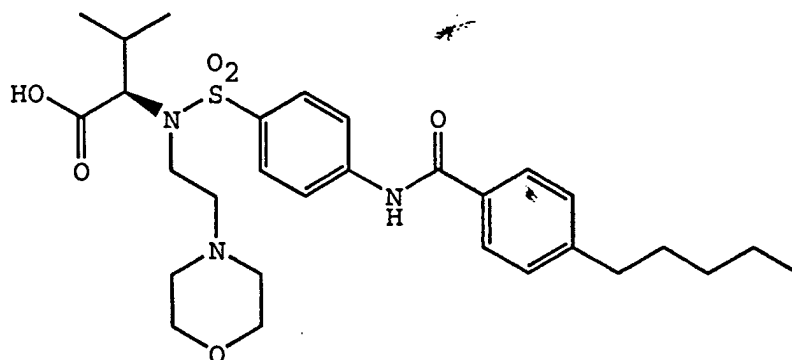
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42. The method of claim 41 wherein  $R^3$  is a  $C_1$  to  
about  $C_{12}$  alkyl.
43. The method of claim 42 wherein  $R^3$  is a  $C_1$  to  
5 about  $C_4$  alkyl.
44. The method of claim 43 wherein  $R^3$  is isopropyl.
45. The method of claim 39 wherein  $R^2$  is  
10 heterocycloalkylalkyl.
46. The method of claim 45 wherein  $R^2$  is 2-(N-  
morpholino)ethyl.
- 15 47. The method of claim 39 wherein  $R^{21}$  and  $R^{25}$  are H.
48. The method of claim 47 wherein  $R^{22}$  and  $R^{24}$  are H.
49. The method of claim 48 wherein  $R^{23}$  is  $C_1$  to about  
20  $C_{20}$  alkyl.
50. The method of claim 49 wherein  $R^{23}$  is methyl or  
 $C_2$  to about  $C_{20}$  linear alkyl.
- 25 51. The method of claim 50 wherein  $R^{23}$  is n-pentyl or  
n-hexyl.
52. The method of claim 51 wherein the compound has  
the structure:

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WO 01/05389

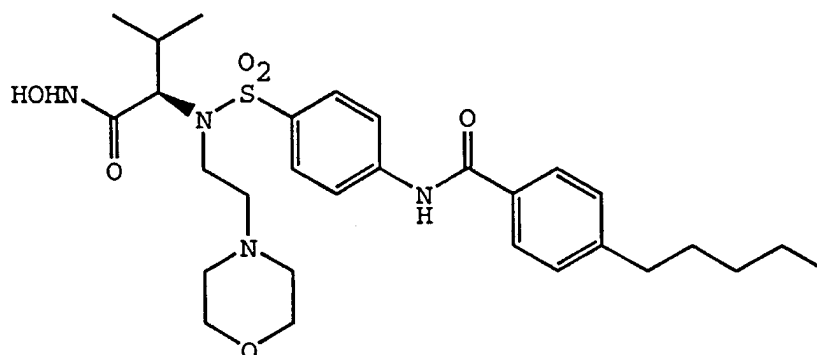
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or a salt, an enantiomer, a racemate, or a tautomer thereof.

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53. The method of claim 51 wherein the compound has the structure:



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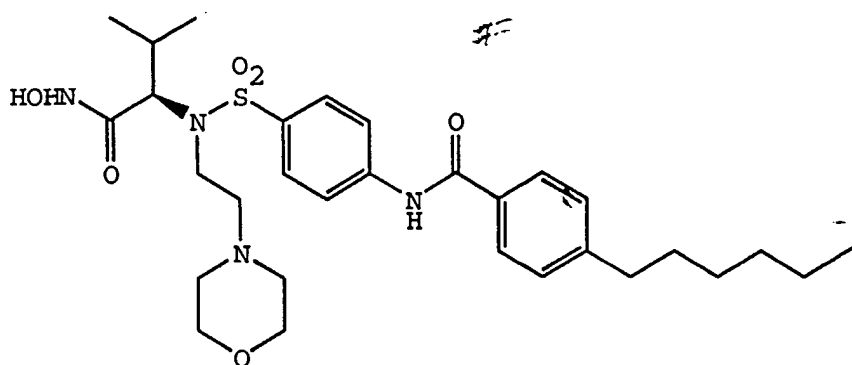
or a salt, an enantiomer, a racemate, or a tautomer thereof.

54. The method of claim 51 wherein the compound has the structure:

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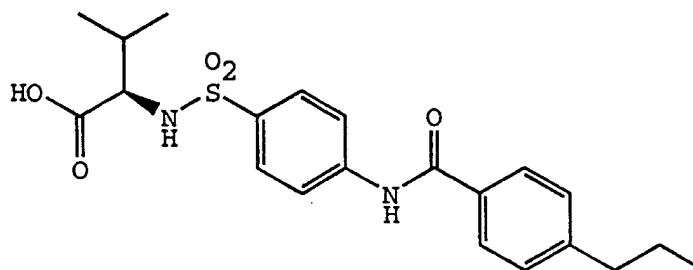
WO 01/05389

PCT/US00/16323



or a salt, an enantiomer, a racemate, or a  
tautomer thereof.

55. The method of claim 51 wherein the compound has  
the structure:



or a salt, an enantiomer, a racemate, or a  
tautomer thereof.

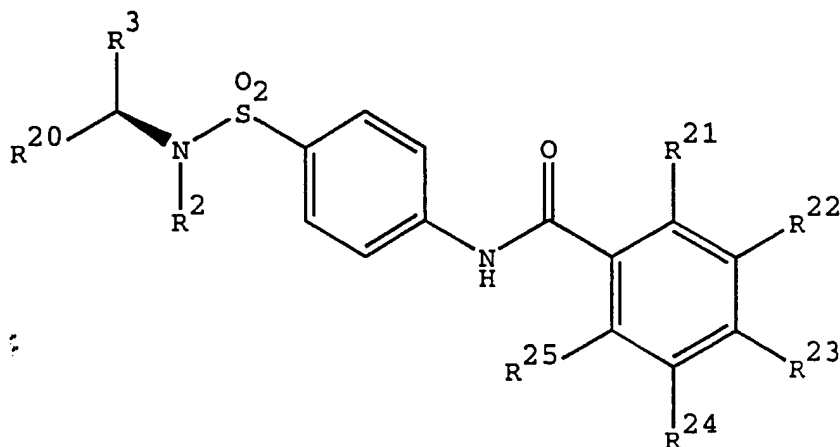
56. The method of claim 39 wherein the matrix  
metalloproteinase is selected from the group  
consisting of MMP-8 and MMP-13.
57. The method of claim 56 wherein the matrix  
metalloproteinase is MMP-8.
58. The method of claim 56 wherein the matrix  
metalloproteinase is MMP-13.

WO 01/05389

PCT/US00/16323

59. A method treating osteoarthritis in a mammal wherein the method comprises providing to the mammal an osteoarthritis-treating-effective amount of a compound having the formula:

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- or an enantiomer, diastereomer, racemate, or tautomer thereof, thereby treating osteoarthritis, wherein:

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R<sup>2</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, alkylaryl, arylalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, heterocycloalkyl, and heterocycloalkylalkyl;

15

R<sup>3</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, alkylaryl, arylalkyl, alkoxy, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, haloalkoxy, haloalkylthio, and heterocycloalkyl;

20

R<sup>20</sup> is selected from the group consisting of -C(O)OH, -C(O)NHOH, -SH, and -C(O)SH; and

R<sup>21</sup>, R<sup>22</sup>, R<sup>23</sup>, R<sup>24</sup>, and R<sup>25</sup> are independently selected from the group consisting of H, C<sub>1</sub> to about C<sub>20</sub> alkyl, C<sub>1</sub> to about C<sub>20</sub> alkenyl, C<sub>1</sub> to about C<sub>20</sub> alkynyl, cycloalkyl, haloalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl,

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WO 01/05389

PCT/US00/16323

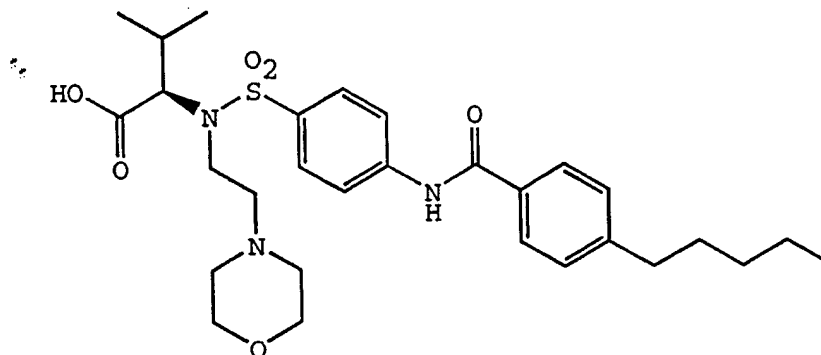
alkylaminoalkyl, nitroalkyl, heterocycloalkyl,  
alkoxy, cycloalkoxy, alkoxycarbonyl,  
alkoxyalkyl, haloalkoxy, haloalkylthio,  
alkylamino, and carboxyalkyl.

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60. The method of claim 59 wherein the mammal is a human.

61. The method of claim 60 wherein the compound has the structure:

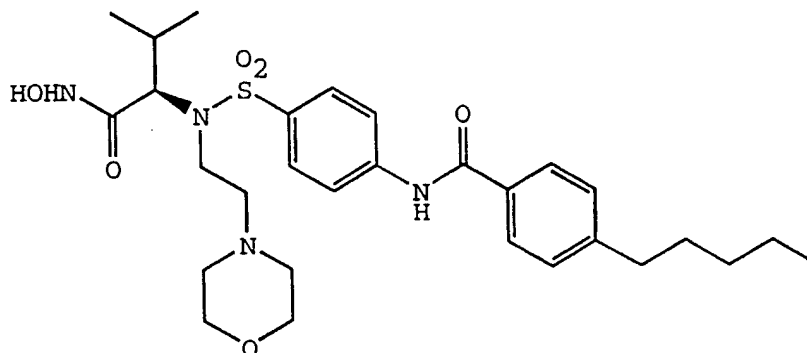
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or a salt, an enantiomer, a racemate, or a tautomer thereof.

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62. The method of claim 60 wherein the compound has the structure:



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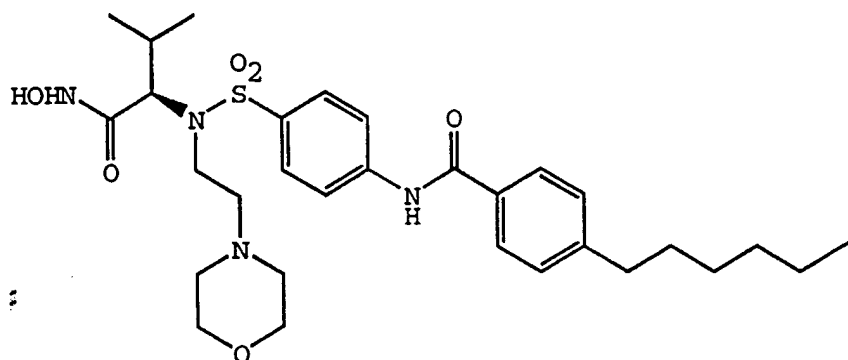
WO 01/05389

PCT/US00/16323

or a salt, an enantiomer, a racemate, or a tautomer thereof.

63. The method of claim 60 wherein the compound has the structure:

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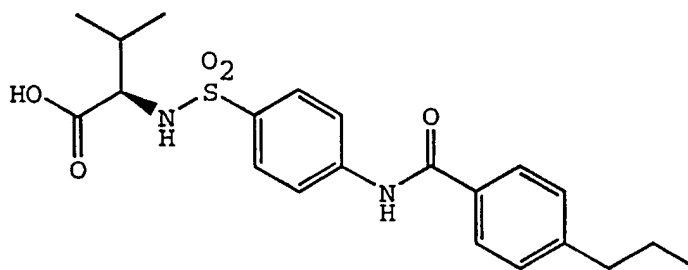


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or a salt, an enantiomer, a racemate, or a tautomer thereof.

64. The method of claim 60 wherein the compound has the structure:

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or a salt, an enantiomer, a racemate, or a tautomer thereof.

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